providing a soluble chimeric construct comprising P-selectin glycoprotein ligand-1 or a fragment thereof and another molecule, said chimeric construct being capable of inhibiting the interaction between P-selectin and a ligand of P-selectin; and

administering to a mammal an effective amount of said chimeric construct such that said P-selectin-ligand interaction is inhibited, wherein said chimeric construct is administered prior to, in conjunction with, or after a vessel-corrective technique.

REMARKS

In the Official Action of June 7, 2002, the Examiner has adhered to the restriction requirement made in the previous Office Action. The Examiner has further requested that applicant submit a clean set of claims that read on the elected invention in Group IV (PSGL-1).

In response, applicants have provided hereinabove a full set of pending, amended claims that are now directed to the elected invention. In addition, applicants have amended the Title of the invention and the Abstract for improved consistency with the amended claims.

Claims 40-41, 45, 49-52 and 73-74 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. This ground of rejection is respectfully traversed,

The Examiner has stated that Claims 40-41, 45 and 49-50 are indefinite by reciting that the method of the invention at least partially prevents or reverses the formation or growth of atherosclerotic lesions in a mammal. This language has now been changed to recite that the method of the invention decreases the formation or growth of atherosclerotic lesions in a mammal.

The Examiner has also stated that the claims are indefinite for reciting P-selectin ligand since this is an arbitrary name. Applicants have now claimed the specific P-selectin ligand P-selectin glycoprotein ligand-1 (PSGL-1). This is a well characterized molecule, as shown in the art, such as Sako et al., *Cell*, 75, pages 1179-1186 (1993). Pages 1 and 2 of Sako et al. identify PSGL-1 as P-selectin glycoprotein ligand-1, and provide both the DNA and amino acid sequences for this protein, as well as further characterizing information. Accordingly, this protein is sufficiently well characterized to obviate any indefiniteness rejection. Basis for this amendment is found in the specification on pages 3 and 10.

Claims 40-41, 45, 49-52, 56, 59-60 and 73-74 have also been rejected under 35 U.S.C. 103(a) as obvious over Cummings et al. (U.S. Patent No. 6,309,639), in view of Tedder et al. (U.S. Patent No. 5,834,425) and Coller et al. (U.S. Patent No. 5,976,532). This ground of rejection is respectfully traversed.

The Examiner states that the Cummings et al. reference teaches clinical applications of PSGL-1, and that reducing leukocyte adherence in ischemic myocardium can significantly enhance the therapeutic efficacy of thrombolytic agents.

The Cummings et al. reference does not disclose the PSGL-1 molecule, or molecular fragments thereof, as recited in the present claims. Cummings et al. simply states that the described ligand is a 120 kD protein that requires sialic acid to interact with P-selectin. See cols. 11 and 12 of the reference. Furthermore, the inhibitory agent used in the reference for inhibiting inflammatory responses, and for inhibiting leukocyte adhesion, is an antibody to a P-selectin glycoprotein ligand. See claims 1 and 2 of the reference.

There is no disclosure in the reference of the treatment of atherosclerosis, of the use of chimeric molecules containing PSGL-1 as one component of the molecule, or in the administration of the chimeric molecule in connection with a surgical procedure. As stated on page 5 of the present specification, atherosclerosis is a condition in which atherosclerotic lesions form on the surface of arterial walls. Atherosclerosis is a long term medical condition, unlike the reperfusion injury condition noted in the reference. Similarly, restinosis is the reclosing of an artery following a coronary angioplasty. Neither atherosclerosis nor restinosis is described in the Cummings et al. reference.

The Examiner has noted some of the deficiencies of Cummings et al. in the Office Action. However, the Examiner has argued that these deficiencies can be overcome by relying on features disclosed in the secondary references to Tedder et al. and Coller et al.

Tedder et al. disclose that chimeric peptides can be formed from the ligand binding regions of two different selectins. However, applicants are claiming a method of using certain chimeric molecules to treat atherosclerosis and restinosis, and have not claimed the chimeric molecules per se.

The Coller et al. reference discloses the use of chimeric platelet-specific antibodies as antithrombotic agents. These agents can be administered in connection with an angioplasty procedure. However, there is no motivation for one skilled in the art to combine the Coller et al.

reference with the Cummings et al. reference which does not mention surgical procedures or chimeric molecules. Furthermore, both the Cummings et al. and Tedder et al. references are directed to inflammatory conditions which are not discussed in Coller et al. Finally, none of the references relate to the treatment of atherosclerosis.

In view of the foregoing facts and reasons, the present application is now believed to overcome the remaining rejections, and to be in proper condition for allowance. Accordingly, reconsideration and withdrawal of the rejections, and favorable action on this application, is solicited. The Examiner is invited to contact the undersigned at the telephone number listed below to discuss the status of this application if necessary.

Respectfully submitted,

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MARKED-UP CLAIMS

40. (Four Times Amended) A method for [at least partially preventing or reversing] decreasing the formation or growth of atherosclerotic lesions in a mammal comprising:

providing a soluble chimeric construct comprising [a P-selectin ligand] P-selectin glycoprotein ligand-1 or a fragment thereof and another molecule, said chimeric construct being capable of inhibiting the interaction between P-selectin and a ligand of P-selectin; and

administering to a mammal an effective amount of said chimeric construct such that said P-selectin-ligand interaction is inhibited, wherein said chimeric construct is administered prior to, in conjunction with, or after a vessel-corrective technique.

51 (Four Times Amended) A method for treating or inhibiting atherosclerosis in a mammal comprising:

providing a soluble chimeric construct comprising [a P-selectin ligand] P-selectin glycoprotein ligand-1 or a fragment thereof and another molecule, said chimeric construct being capable of inhibiting the interaction between P-selectin and a ligand of P-selectin; and

administering to a mammal an effective amount of said chimeric construct such that said P-selectin-ligand interaction is inhibited, wherein said chimeric construct is administered prior to, in conjunction with, or after a vessel-corrective technique.

73. (Amended) A method for treating restinosis in a mammal to which a vessel-corrective technique is administered comprising:

performing a vessel-corrective technique selected form the group consisting of angioplasty, stenting procedure, atherectomy, and bypass surgery on a mammal; and

administering to said mammal, prior to, in conjunction with or after said vessel-corrective technique, an effective amount of a soluble chimeric construct comprising [a P-selectin ligand] P-selectin glycoprotein ligand-1 or a fragment thereof, and another molecule, said chimeric construct being capable of inhibiting the interaction between P-selectin and a ligand of P-selectin, such that the restinosis occurring after said vessel-corrective technique is thereby treated.

74. (Amended) A method for treating restinosis in a mammal, comprising:

providing a soluble chimeric construct comprising [a P-selectin ligand] P-selectin glycoprotein ligand-1 or a fragment thereof and another molecule [capable], said chimeric construct being capable of inhibiting the interaction between P-selectin and a ligand of P-selectin; and

administering to a mammal an effective amount of said chimeric construct such that said P-selectin-ligand interaction is inhibited, wherein said chimeric construct is administered prior to, in conjunction with, or after a vessel-corrective technique.